Recurrent malignant melanoma detected on fluciclovine (^{18}F) PET/CT imaging for prostate cancer

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Short title as running head:

Melanoma recurrence detected on fluciclovine PET (43 characters)

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Conflict of interest

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Unstructured abstract

A 66-year-old man presented with biochemical recurrence of prostate cancer and underwent fluciclovine (^{18}F) PET/CT to detect sites of recurrence. He had a history of resected truncal stage IIIC malignant melanoma, with bilateral axillary node involvement on sentinel node biopsy, in complete remission for 3 years.

Fluciclovine (^{18}F) PET/CT demonstrated an incidental fluciclovine-avid right axillary node (SUV_{max}=4.3). Diagnostic sampling confirmed recurrent malignant melanoma.

Figure legend

A 66-year-old man with a history of radical prostatectomy for prostate cancer, presented with biochemical recurrence (prostate specific antigen level 0.32 ng/ml) and underwent fluciclovine (^{18}F) PET/CT to detect sites of disease recurrence. He also had a history of resection of a truncal stage IIIC 4-mm non-ulcerated malignant melanoma, with bilateral axillary node involvement on sentinel node biopsy, in complete remission for 3 years. While the site of prostate cancer recurrence was not demonstrated, an incidental fluciclovine-avid (SUV_{max}=4.3) 12-mm right axillary node was detected. Diagnostic sampling and subsequent right axillary node dissection two months later confirmed recurrent malignant melanoma.

Fluciclovine (^{18}F) / anti-1-amino-3-[^{18}F]-fluorocyclobutane-1-carboxylic acid (FACBC) is a synthetic amino acid, recently FDA-approved for imaging recurrent prostate cancer[1]. It is predominantly transported into cells by high-affinity glutamine transporter ASCT2, and leucine transporter LAT1[2, 3]. There has been therapeutic interest in targeting glutamine metabolism by utilising ASCT2 inhibitors in melanoma[4] as well as prostate cancer[5], which in the case of melanoma, is fuelled by observation of a metabolic switch to glutamine dependence on developing resistance to BRAF inhibition[6, 7]. Disease detection aside, this raises potential application in patient selection and response assessment to such emerging therapies.

Unlike fluorodeoxyglucose, which demonstrates non-specific uptake upon activation of both innate and adaptive immune response components, preclinical studies report uptake of fluciclovine only upon T- and B-cell activation, but not in granulocytes and macrophages[8]. Fluciclovine may therefore have the potential ability to selectively image T-cell modulation in the tumour microenvironment.

References

1. FDA approves new diagnostic imaging agent to detect recurrent prostate cancer. U.S. Food and Drug Administration [Internet]. 2016 [cited 19 May 2017]. Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm503920.htm

2. Oka S, Okudaira H, Yoshida Y, et al. Transport mechanisms of trans-1-amino-3-fluoro[1-(14)C]cyclobutanecarboxylic acid in prostate cancer cells. *Nucl Med Biol*. 2012;39:109-119.

3. Okudaira H, Shikano N, Nishii R, et al. Putative transport mechanism and intracellular fate of trans-1-amino-3-18F-fluorocyclobutanecarboxylic acid in human prostate cancer. *J Nucl Med*. 2011;52:822-829.

4. Wang Q, Beaumont KA, Otte NJ, et al. Targeting glutamine transport to suppress melanoma cell growth. *Int J Cancer*. 2014;135:1060-1071.

5. Wang Q, Hardie RA, Hoy AJ, et al. Targeting ASCT2-mediated glutamine uptake blocks prostate cancer growth and tumour development. *J Pathol*. 2015;236:278-289.

6. Baenke F, Chaneton B, Smith M, et al. Resistance to BRAF inhibitors induces glutamine dependency in melanoma cells. *Mol Oncol*. 2016;10:73-84.

7. Villanueva J, Vultur A, Herlyn M. Resistance to BRAF inhibitors: unraveling mechanisms and future treatment options. *Cancer Res*. 2011;71:7137-7140.

8. Oka S, Okudaira H, Ono M, et al. Differences in transport mechanisms of trans-1-amino-3-[18F]fluorocyclobutanecarboxylic acid in inflammation, prostate cancer, and glioma cells: comparison with L-[methyl-11C]methionine and 2-deoxy-2-[18F]fluoro-D-glucose. *Mol Imaging Biol*. 2014;16:322-329.

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